## REMARKS

As the Applicants elected with traverse the Claims of Group II, Claims 15-19, the Examiner has considered only claims 15-19 in the Office Action of November 4, 2003 and has rejected Claims 15-19.

## Rejection under 35 U.S.C. § 102.

The Examiner has rejected Claims 15-16 under 35 U.S.C. 102(b) as being anticipated by Bryan et al. U.S. Patent 6,232,107 ("Bryan"). Bryan is directed to fusion proteins comprising green fluorescent proteins (GFP) and luciferase and their use in luciferase based assays.

Applicants assert that Bryan does not anticipate present invention for at least the following reasons. Luciferase based assays are well known in the art to have some very specific and well known features and applications. That luciferase assays are broadly representative of biologically assays is at the least questionable in view of the unique features of luciferase. Also, GFP is a much simpler fluorescent protein than phycobiliprotein. The only references to phycobiliprotein are very generalized comments which provide no teaching for incorporating or utilizing the more complex phycobiliproteins in a fusion protein.

Further, Bryan teaches the use of luciferase as the second domain of the fusion proteins.

Luciferase is an enzyme. It is well known that an enzyme is an entity which facilitates a reaction but is not changed by the reaction. In contrast Independent Claim 15 as it currently stands states:

"In a method for biologic activity assays to determine a particular entity which induces a known biologic effect, the improvement comprising using a detectable label which is a fusion protein containing a phycobiliprotein domain and a second domain which undergoes the known biologic effect upon encountering the particular entity, wherein the known biologic effect induces a detectable change in the fusion protein (emphasis added)."

Accordingly, Claim 15 is directed to a fusion protein with a second domain that undergoes detectable change upon an encounter. An enzyme second domain which by definition would not be changed by an encounter does not fulfill the requirements of Claim 15.

The Examiner has cited Bryan Col. 7, lines 25-35 and Col. 6, line 30-40 for disclosing use of fusion proteins in analytical assays and screening methods. Applicants respectfully direct the Examiners attention to the fact that Claim 15 is "for an improvement comprising." Accordingly, the Applicants assert that Claim 15 claims an improved method for biological assays. The passages of Bryan cited by the Examiner do not disclose the improvement of the present invention.

For at least the reasons that Bryan (1) provides enabling teaching for preparing and using a fusion protein comprising simple GFP but not for other florescent proteins, especially not for a more complex fluorescent protein such as a phycobiliprotein, (2) Bryan is directed to the very specific system of GFP and luciferase; and (3) Bryan discloses a fusion protein in which the second domain is an enzyme, an entity characterized by its lack of change as the result of reactive encounters, the applicants submit that Bryon does not anticipate Claims 15 and 16 under 35 U.S.C. 102 (e). Accordingly, applicants respectfully request that the Examiner withdraw her rejection of Claims 15-16.

## Rejection - Under 35 U.S.C. § 103

The Examiner has rejected Claim 17-19 under 35 U.S.C. 103(a) as assertly unpatentable over Bryan. The Examiner states that Bryan teaches fusion proteins utilizing luciferase as a second domain to catalyze substrates and that it would be obvious

to modify Bryan to include "using known enzymes such as a ribozyme, phosphokinase or a protease."

As discussed in detail above the second domain of the fusion protein of Claim 15 and its dependent Claims 16-19, is not an enzyme. In fact, Claim 16 specifically claims the second domain that is "a substrate for an enzyme." Accordingly, as claimed in Claims 16-19, the fusion protein has a first domain that is a phycobiliprotein and a second domain that is an enzyme substrate, and the enzymes referenced in dependent Claims 17-19 are the "particular entity" which is the analyte detected by the method of independent Claim 15. Claims 16-17 are directed to a method for detecting enzymes not to methods using an enzyme as an assay tool.

Bryan provides no teaching or suggestion for using the substrate of an enzyme as the second domain of the fusion protein. In fact, Bryan is very narrowly focused not only on using an enzyme as the second domain, but also the specific enzyme luciferase.

Clearly since Bryan is directed to utilizing an enzyme as an assay tool and claims 17-19 are directed to a method for detecting enzymes, there is no prima facie case of obviousness for Claims 17-19.

For the reasons discussed above in detail Applicants submit that Bryan does not render Claims 17-19 obvious under 35 U.S.C. 103(a). Applicants respectfully request that the Examiner withdraw her rejection of Claims 17-19.

## **CONCLUSION**

For at least the reasons set forth above, Applicants respectfully submit that claims 15-19 are in condition for allowance. Applicants therefore request that the claims be allowed.

It is believed that no fees are due with this response. However, if any additional fees are determined to be due, the Director is hereby authorized to charge these fees to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

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